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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.
09/402,277	09/30/99	KAWASHIMA E	018428-00030

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WILLIAM M SMITH
TOWNSEND AND TOWNSEND AND CREW
TWO EMBARCADERO CENTER
8TH FLOOR
SAN FRANCISCO CA 94111-3834

EXAMINER	
LU, F	

ART UNIT	PAPER NUMBER
1655	13

DATE MAILED: 04/24/01

Please find below and/or attached an Office communication concerning this application or proceeding.

Commissioner of Patents and Trademarks

1- File Copy

PTO-90C (Rev.11/00)

Office Action Summary

Application No.	Applicant(s)
09/402,277	Kawashima et al.,
Examiner	**Group Art Unit**
Frank Lu	1655

☒ Responsive to communication(s) filed on *12/19/2000 and 1/23/2001*.

☒ This action is **FINAL**.

☐ Since this application is in condition for allowance except for formal matters, **prosecution as to the merits is closed** in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11; 453 O.G. 213.

A shortened statutory period for response to this action is set to expire *3* month(s), or thirty days, whichever is longer, from the mailing date of this communication. Failure to respond within the period for response will cause the application to become abandoned. (35 U.S.C. § 133). Extensions of time may be obtained under the provisions of 37 CFR 1.136(a).

Disposition of Claims

☒ Claim(s) *1-30 and 59-65* is/are pending in the application.

Of the above, claim(s) *27-30 and 65* is/are withdrawn from consideration.

☐ Claim(s) _____ is/are allowed.

☒ Claim(s) *1-26 and 59-64* is/are rejected.

☐ Claim(s) _____ is/are objected to.

☐ Claims _____ are subject to restriction or election requirement.

Application Papers

☐ See the attached Notice of Draftsperson's Patent Drawing Review, PTO-948.

☐ The drawing(s) filed on _____ is/are objected to by the Examiner.

☐ The proposed drawing correction, filed on _____ is ☐approved ☐disapproved.

☐ The specification is objected to by the Examiner.

☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. § 119

☒ Acknowledgement is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d).

☒ All ☐ Some* ☐ None of the CERTIFIED copies of the priority documents have been

☒ received.

☐ received in Application No. (Series Code/Serial Number) _____.

☐ received in this national stage application from the International Bureau (PCT Rule 17.2(a)).

*Certified copies not received: _____.

☐ Acknowledgement is made of a claim for domestic priority under 35 U.S.C. § 119(e).

Attachment(s)

☒ Notice of References Cited, PTO-892

☐ Information Disclosure Statement(s), PTO-1449, Paper No(s). _____

☐ Interview Summary, PTO-413

☐ Notice of Draftsperson's Patent Drawing Review, PTO-948

☐ Notice of Informal Patent Application, PTO-152

--- SEE OFFICE ACTION ON THE FOLLOWING PAGES ---

DETAILED ACTION

Response to Amendment

1. Applicant's response to the office action filed on December 19, 2000 has been entered as Paper No: 10. The claims pending in this application are claims 1-30 and 59-65 with nonelected claims 27-30 and 65.. Rejection and/or objection not reiterated from the previous office action has been hereby withdrawn.

Election/Restriction

2. Applicant's election with traverse of Group I, claims 1-26 and 59-64 in Paper No. 10 is acknowledged. The traversal is on the ground(s) that: (1)"restricted claims are closely related that they should remain in the same application to preserve unity of invention" (page 11, last paragraph of applicant's remark); and " it is natural and reasonable and desirable to search prior art for these claims together" since " the claims are closely related".

The above arguments have been fully considered and have not been found pervasive toward the withdrawal of the restriction requirement nor pervasive toward the relaxation of same such that Groups I and II will be examined together. First, Groups I and II do not relate to a single general inventive concept under PCT Rule 13.1 since, under PCT Rule 13.2, they lack the same or corresponding special technical features. In other words, Groups I and II are distinct from each other. For example, the products in Group II can be used in a materially different process such as a hybridization assay. Second, there is a search burden on the examiner. For example, the examination of Groups I did not include to search the density of immobilized nucleic

acid on the surface as described in claim 30 and a kit for use in screening, diagnosis or in nucleic acid sequencing as described in claim 65.

Therefore, the requirement is still deemed proper and is therefore made FINAL.

3. This application contains claims 27-30 and 65 drawn to an invention nonelected with traverse in Paper No. 8. A complete reply to the final rejection must include cancellation of nonelected claims or other appropriate action (37 CFR 1.144) See MPEP § 821.01.

Drawings

4. Applicant's request that "applicant will correct any defects in the drawings upon a notice of allowable subject matter" has been granted by the examiner.

Sequence Rules Compliance

5. The sequencing listing submitted on February 23, 2001 has complied with Requirements For Patent Applications Containing Nucleotide Sequence And/Or Amino Acid Sequence Disclosures.

Claim Rejections - 35 U.S.C. § 112

6. The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

7. Claim 62 is rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 62 is rejected as vague and indefinite over the phrase "so that another nucleic acid strand is located on the surface within a distance of the length of that strand " because it is unclear what "that strand" means here. For example, does "that strand " mean said each nucleic acid single strand or said plurality of nucleic acid single strands?

Response to Arguments

In page 15, fourth paragraph, applicant argued that there was no lack of clarity in the meaning of "that strand".

This argument has been fully considered but it is not persuasive toward the withdrawal of the rejection because this issue was not used for the rejection because, although applicant pointed out that "the meaning of that strand is the identical nucleic acid strand or identical complementary strand", it is unclear that "that strand " mean said each nucleic acid single strand or said plurality of nucleic acid single strands.

Claim Rejections - 35 U.S.C. § 103

8. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person

having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CAR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(f) or (g) prior art under 35 U.S.C. 103(a).

9. Claims 1-18, 21-26, and 59-64 are rejected under 35 U.S.C. 103(a) as being unpatentable over Hosoi *et al.*, (European Patent No: 665293 A2, published on February 8, 1995) in view of Cheng *et al.*, (Nucleic Acids Res. 24, 380-395, January 1996).

Hosoi *et al.* teach: (1) hybridizing each of plural primers with a template comprising a single-stranded nucleic acid to form complex having a double-stranded portion comprising a portion of the template and the primer, the plural primers being separately disposed in a plurality of regions in accordance with the kinds of the primers; (2) substantially simultaneously adding plural kinds of nucleotides or nucleotide analogues to the complexes respectively disposed in the plural regions, thereby to perform growth reaction of the primer with the nucleic acid to be examined as the template in a direction of from 5' to 3' of the primer, the plural kinds of nucleotides or nucleotide analogues being complementary to nucleotides constituting the template in the complex, and being capable of forming base pair with nucleotides constituting the template; (3) detecting the amount of the growth of the primers (see abstract); (4) a plurality of

oligonucleotides including all of the combinations as plural primers were fixed into plural columns in a capillary plate (AC) with a square shape (Figure 1); (5) four different fluorescent-dNTP as tags; (6) a detection apparatus comprising a charge coupled device (page 14, second paragraph and a magnify device (page 16, third paragraph, method step (III)). For example, trimers (3 mers) of all of the combinations containing A, T, G, and C, were fixed into 64 columns of the glass capillary plate, as shown in Figure 8 (page 13, fifth paragraph). The primer disposed in each column was hybridized with the nucleic acid to be examined. The nucleic acid to be examined which has not been hybridized with the primer was washed out (page 13, sixth paragraph), then four kind of fluorescent-dNTPs were simultaneously added together with DNA polymerase, a unidirectional extension reaction of each of the primers occurred in the direction corresponding to the direction of from 5' to 3' of the primer (see Figure 9B) (page 13, seventh paragraph). After the reaction, the resultant capillary plate CA was placed in a dark DB box as shown in Figure 10A, which constituted an apparatus for determining the base sequencing of nucleic acid. The apparatus as shown in Figure 10A comprised: (1) the dark box DB1 for housing the capillary plate CA so as to shut off external light; (2) an excitation light source 70 (such as Xenon lamp) for supplying excitation light to the capillary plate CA; and (3) a CCD television camera 10 disposed on a surface on side of the dark box DB1, for picking up an image of the capillary plate CA (page 14, second paragraph). Note that sequencing reactions were performed by incubating the above test tube at 95^0 C (30 seconds), at 41^0 C (30 seconds), and at 72^0 C (5 minutes) (page 15).

Hosoi *et al.*, do not disclose performing PCR on the solid support as described in the steps (C) to (E) of claim 1, claims 2, 14-16, 23, and 60.

Cheng *et al.*, do teach performing PCR on microfabricated silicon-glass chips using Taq DNA polymerase. The general PCR principle from this reference clearly teach the steps (C) to (E) of claim 1, claims 2, 14-16, 23, and 60. They examined PCR on silicon dioxide-coated silicon-glass chips using two PCR reagent systems: (1) the conventional reagent system using Taq DNA polymerase; (ii) the hot-start reagent system based on a mixture of TaqStart antibody and Taq DNA polymerase. Quantitative results obtained from capillary electrophoresis for the expected amplification products showed that amplification on microchips was reproducible and provided excellent yields (page 380, abstract).

Therefore, in the absence of an unexpected result, it would have been *prima facie* obvious to one having ordinary skill in the art at the time the invention was made to have performed PCR on the solid support such as a capillary plate immobilized with a plurality of identical or different primers using single stranded nucleic acid templates and fluorescent-dNTPs as suggested by Cheng *et al.*, and detected signals from PCR products using an apparatus comprising a CCD camera and a magnifying device as suggested by Hosoi *et al.*. One having ordinary skill in the art would have been motivated to modify and combine above methods together because the sequencing apparatus with temperature range (41 °C-95 °C) made by Hosoi *et al.*, reasonably suggested its application in PCR since only difference between the sequencing reaction performed by Hosoi *et al.*. and PCR was that PCR contained two or more repeating circles.

Furthermore, the simple replacement of one solid support from another solid support such as a solid support immobilized with a plurality of identical or different primers in PCR would have been, in the absence of an unexpected result, *prima facie* obvious to one having ordinary skill in the art at the time the invention was made. As regards the motivation to make the substitution cited above, the motivation to combine arises from the expectation that the prior art elements will perform their expected functions to achieve their expected results when combined for their common known purpose. Support for making the obviousness rejection comes from the M.P.E.P. at 2144.07 and 2144.09.

Also note that there is no invention involved in combining old elements is such a manner that these elements perform in combination the same function as set forth in the prior art without giving unobvious or unexpected results. *In re Rose* 220 F.2d. 459, 105 USPQ 237 (CCPA 1955).

10. Claims 19 and 20 are rejected under 35 U.S.C. 103(a) as being unpatentable over Hosoi *et al.*, (1995) and Cheng *et al.*, (1996) as applied to claims 21-26, and 59-64 above, and further in view of and Hahn *et al.*, (Anal. Biochem. 229, 236-248, August 1995).

The teachings of Hosoi *et al.*, and Cheng *et al.*, have been summarized previously, *supra.*

Hosoi *et al.*, and Cheng *et al.*, do not disclose the digestion of PCR product using a restriction enzyme as described in claims 19 and 20.

Hahn *et al.*, do teach the digestion of PCR product using a suitable restriction enzyme (see abstract in page 236).

Therefore, in the absence of an unexpected result, it would have been *prima facie* obvious to one having ordinary skill in the art at the time the invention was made to have released an immobilized nucleic acid molecule or part thereof using a suitable restriction enzyme as suggested by Hahn *et al.*. One having ordinary skill in the art would have been motivated to modify the method of Hosoi *et al.*, and Cheng *et al.*, and combine above methods together because restriction digestion would have provided a nice way to release an immobilized nucleic acid molecule or part thereof . It has been well know to cut DNA with a restriction enzyme, one having ordinary skill in the art at the time the invention was made would have been a reasonable expectation of success to combine these methods together because all of these method are known in the art and are easy to use.

Response to Arguments

I. In page 16, third paragraph bridging to page 17, second paragraph of applicant's remarks, applicant argued that: (1) " there is nothing in Hosoi to suggest providing pairs of PCR primers in immobilized form located sufficiently close to each other (with the length of an extended primer) so that an extended immobilized primer can act as a template for further rounds of amplification in an immobilized system"; and (2) "the method of Hosoi could not be used for the present invention (where forward and reverse PCR primers would needed to be located very close to one other on the surface, i.e., not at separate locations).

These arguments have been fully considered but they are not persuasive toward the withdrawal of the rejection. In response to applicant's arguments that the references fail to show certain features of applicant's invention, it is noted that the features upon which applicant relies

(i.e., pairs of PCR primers in immobilized form located sufficiently close to each other) are not recited in the rejected claim(s). Although the claims are interpreted in light of the specification, limitations from the specification are not read into the claims. See *In re Van Geuns*, 988 F.2d 1181, 26 USPQ2d 1057 (Fed. Cir. 1993).

II. In page 17, third paragraph of applicant's remarks, applicant argued that " in order to sequence a molecule according to Hosoi et al., all possible primers against a given region must be made and placed in precisely defined separate regions. Thus, the plates used in Hosoi et al., for sequencing are expensive and time-consuming to manufacture".

This argument has been fully considered but it is not persuasive toward the withdrawal of the rejection because this issue was not related to the rejection.

III. In page 17, fourth paragraph bridging to page 18, eighth paragraph, applicant argued that both references of Cheng et al., and Hahn et al., teach away from the presently claimed methods because: (1) the chip in Cheng et al., "are not used for immobilization of primers on the surface, but for different purpose"; (2) "Cheng et al., are not intended to be used to immobilize PCR reagents"; (3) Cheng et al., recommends to prevent non-specifically binding to the glass surface of the microchip using an antibody; and (4) "immobilization is used in Hahn et al., for a completely different purpose from the present invention and PCR is performed within a fluid environment rather than on a surface".

These arguments have been fully considered but they are not persuasive toward the withdrawal of the rejection because the rejection was not based on the solid supports used by Cheng et al., and Hahn et al., (see above the rejection under 35 U.S.C. 103(a)).

Conclusion

11. **THIS ACTION IS MADE FINAL.** Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

12. No Claim is allowed.

13. Papers related to this application may be submitted to Group 1600 by facsimile transmission. Papers should be faxed to Group 1600 via the PTO Fax Center located in Crystal Mall 1. The faxing of such papers must conform with the notices published in the Official Gazette, 1096 OG 30 (November 15, 1988), 1156 OG 61 (November 16, 1993), and 1157 OG 94 (December 28, 1993)(See 37 CAR § 1.6(d)). The CM Fax Center number is either (703) 308-4242 or (703)305-3014.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Frank Lu, Ph.D., whose telephone number is (703) 305-1270. The examiner can normally be reached on Monday-Friday from 9 A.M. to 5 P.M.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, W. Gary Jones, can be reached on (703) 308-1152.

Any inquiry of a general nature or relating to the status of this application should be directed to the Chemical Matrix receptionist whose telephone number is (703) 308-0196.

Frank Lu
April 23, 2001

W. Gary Jones
Supervisory Patent Examiner
Technology Center 1600
4/23/01